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Porous alumina ceramic as a bone scaffold with antibacterial qualities

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Background: Bone infections are difficult to treat as diffusion of antibiotics is low. This is even truer when a foreign body is inserted due to the presence of a biofilm protecting bacteria. Local delivery of antibiotics could be an answer however current techniques such as antibiotic loaded cement present several pitfalls. Indeed, cement needs to be removed, it is subject to infection and the amount of antibiotic released is low (less than 10% in the literature) and not well characterized.

We developed an alumina based ceramic which can be loaded with antibiotics and acts like a scaffold for bone osseointegration. Indeed, alumina is known for its great biocompatibility and the compressive strength of our product is 3 times greater than native cancellous bone. We present here its main antibacterial characteristics such as a poor colonization and its ability to release high amount of antibiotic.

Material/methods: Two studies were performed:

- Cubes (n=3 for each material) made of ceramic and other biomaterial used in orthopedic surgery (stainless-steel, titanium, and polyethylene) were soaked in bacterial suspension containing either *Staphylococcus aureus* (CIP76.25) or *Pseudomonas aeruginosa* (CIP76.110) which are known to produce biofilm. Counting of adherent bacteria was determined after 3 washing steps and sonication of each cube. Results were linked to the surface of each material as the porous structure possesses an exposed surface 16 times greater than plain cubes.
- Different shapes and volumes of ceramic were loaded with either gentamicin or vancomycin and release curves were performed *in vitro* in physiological serum.

Results: Bacterial adherence was significantly lower on ceramic than on titanium ($p=0.01$), stainless-steel ($p=0.02$) or polyethylene ($p<0.01$) for *P. aeruginosa* and for *S. aureus* on polyethylene ($p=0.01$). This is in line with what we observed *in vivo* as only one infection occurred among more than 6000 implantations of this ceramic in humans (intersomatic cervical cages, tibial osteotomy wedge, etc ...) since twenty years. To date there is no clear explanation for this low adherence, even with bacteria known to produce biofilm.

Antibiotic release was complete (conversely to cement) and was achieved between 1 and 3 days depending on the volume and the size of each element. Furthermore, in an about 30cm³ piece, the gentamicin dose included was the same of a usual daily dose (approximately 300 mg), meaning that a large amount of antibiotic would be released at the time of implantation.

Conclusions: This porous alumina ceramic possesses 2 main characteristics for its protection against infection during its implantation: 1) a lower adhesion of bacteria on its surface, even with strains producing biofilm, 2) the delivery of a high local concentration of antibiotics during the first hours and days when the bacterial colonization may occur.